Appendix 4
(just front page)

United States Patent [19]

Hansen et al.

US005874540A

[11] Patent Number:

5,874,540

[45] Date of Patent:

Feb. 23, 1999

[54]	CDR-GRAFTEI TYPE MI ANTI-CEA
	HUMANIZED I IOUSE MONOCLONAL
	ANTIBODIES

- [75] Inventors: Hans J. Hansen, Mystic Island, N.J.; Kath: yn L. Armour, Aberdeen,
- [73] Assignce: Imm nomedies, Inc., Morris Plains, N.J.
- [21] Appl. No.: 318,1. 7
- [22] Filed: COct 1, 1994

[56] Rei stences Cited

U.S. PAT INT DOCUMENTS

		rinus et al 436/518
5,081,235	1/1992	hively et al 536/27
5,530,101	6/1996	tueen et al 530/387 3

FOREIGN PATENT DOCUMENTS

0 239 400 9/1987 European Pat. Off. ____ C12N 15/00

0 323 805 A2 7/1989 0 323 806 12/1989 92/01059 1/1992 WO 92/01059 1/1992	European Pat. Off WIPO
---	------------------------

OTHER PUBLICATIONS

Primus et al., "Immunological Heterogeneity of Carcinoembryonie...", Cancer Research, 43:686–92, Feb. 1983.

Hansen et al., "Characterization of Second-Generation Monocional...", Cancer, 71(11):3478–85, Jun. 1993.

Losman et al., "Mimicry of a Carcinoembryonic Antigen Epitope...", Int. J. Cancer, 56:580–84, 1994.

Sharkey et al. [Cancer 71(6):2082–2096 (1993)].

Ricchmann et al. [Nature 332:323–327 (1988)].

Queen et al. [PNAS 86:10029–10033 (1989)].

Bhumenthal et al. [Cancer Res 52(21):6036–6044 (1992)].

Primary Examiner—Frank C. Eisenschenk Attorney, Agent, or Firm—Foley & Lardner

7] ABSTRACT

A humanized monoclonal antibody, comprising the complementanty-determining regions of a parental murine Class III, anti-CEA monoclonal antibody engrafted to the framework regions of a beterologous antibody, wherein the humanized monoclonal antibody retains the binding specificity of, but is less immunogenic in a heterologous host than, the parental murine monoclonal antibody A preferred murine Class III, anti-CEA monoclonal antibody is the MN-14 antibody and the preferred heterologous antibody is from a human. Also provided are DNA constructs and vectors for producing the humanized monoclonal antibodies, and diagnostic and therapeutic conjugates using same.

30 Claims, 16 Drawing Sheets